

A tropical beach scene with a thatched hut on a pier in the background, framed by palm fronds. The water is a clear turquoise color, and the sky is a pale blue. The foreground shows a sandy beach with some green foliage on the left.

**The biotechnological challenge: Exploiting
the Opportunities and managing the risks**

Biological Challenge - Infectious Diseases

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Washington DC, 10-11 December 2002

Events that Focused Concern on Possible Terrorist Attacks Against the United States

1982 - Packages of Tylenol contaminated with cyanide

1984 - *Salmonella* contamination of salad bars by the Rajneesh cult

1995 - Aum Shinrikyo nerve gas attack on Tokyo subway

Uncovering of advanced biological weapons programs in Iraq and former Soviet Union

2001 - Attacks on World Trade Center, Pentagon

2001 - Anthrax incidents in various U.S. cities

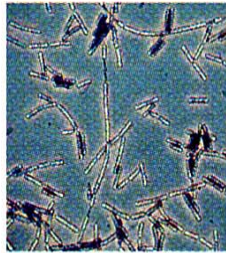
Microorganisms as bioagents



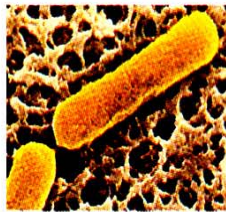


Conventional BW agents

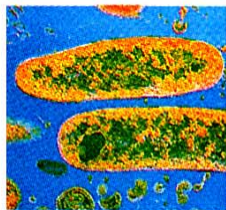
Potential Biological Agents



Bacillus anthracis. Causes anthrax. If bacteria are inhaled, symptoms may develop in two to three days. Initial symptoms resembling common respiratory infection are followed by high fever, vomiting, joint ache and labored breathing, and internal and external bleeding lesions. Exposure may be fatal. Vaccine and antibiotics provide protection unless exposure is very high.



Botulinum toxin. Cause of botulism, produced by *Clostridium botulinum* bacteria. Symptoms appear 12 to 72 hours after ingestion or inhalation. Initial symptoms are nausea and diarrhea, followed by weakness, dizziness and respiratory paralysis, often leading to death. Antitoxin can sometimes arrest the process.



Yersinia pestis. Causes bubonic plague, the Black Death of the Middle Ages. If bacteria reach the lungs, symptoms—including fever and delirium—may appear in three or four days. Untreated cases are nearly always fatal. Vaccines can offer immunity, and antibiotics are usually effective if administered promptly.



Ebola virus. Highly contagious and lethal. May not be desirable as a biological agent because of uncertain stability outside of animal host. Symptoms, appearing two or three days after exposure, include high fever, delirium, severe joint pain, bleeding from body orifices, and convulsions, followed by death. No known treatment.

Biological Warfare against Crops

*Intentionally unleashing organisms that kill an enemy's food crops
is a potentially devastating weapon of warfare and terrorism*





Food born diseases



TARGET FOR TERROR Salad bars like this one in New York City could easily be contaminated with dangerous pathogens like salmonella that would make anyone who ate from them dangerously ill



First Shot in Biological Warefare

scientific correspondence

Deadly relic of the Great War



Figure 1 Sugar lumps with an embedded glass capillary shown to contain spores of *Bacillus anthracis*.

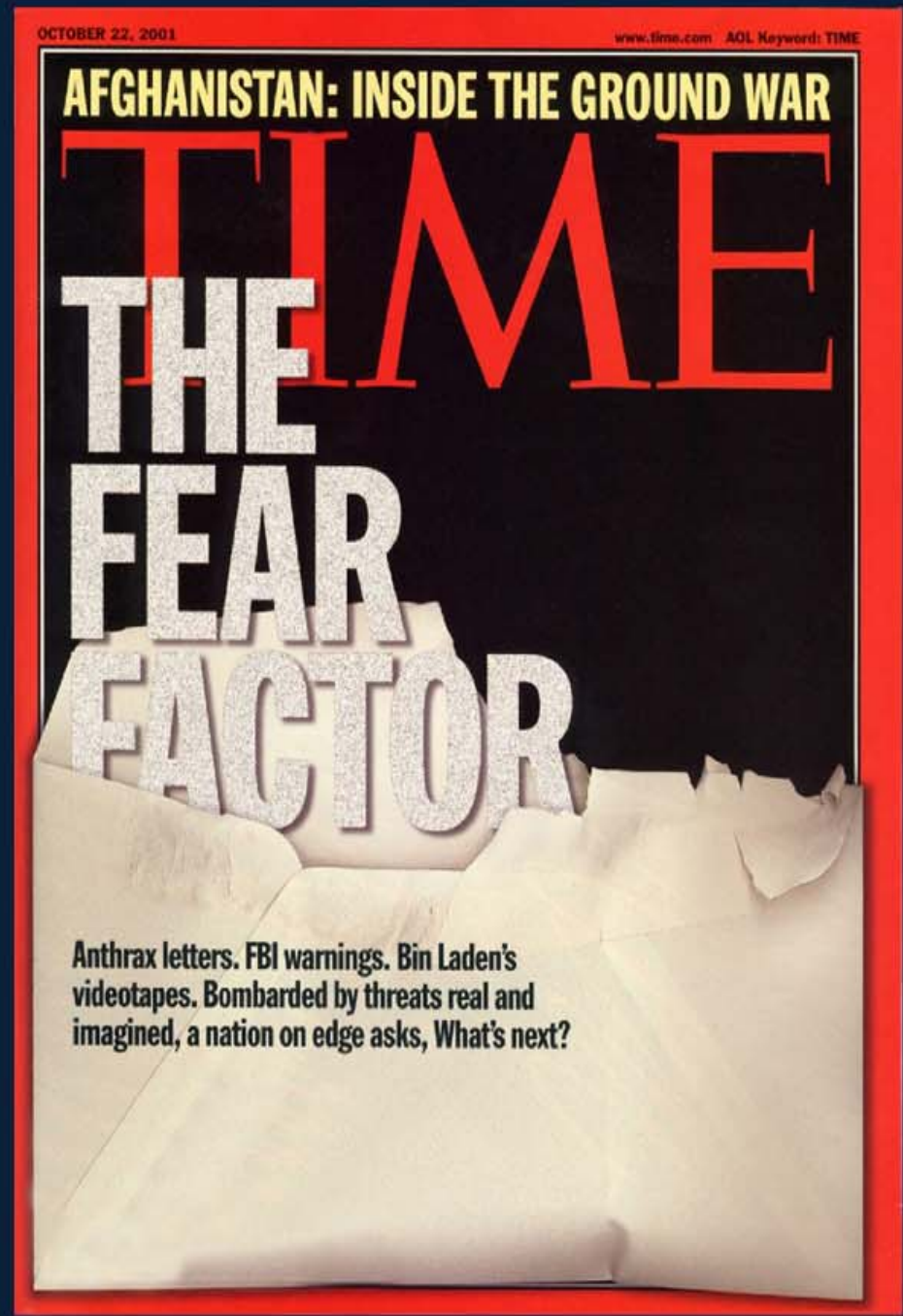
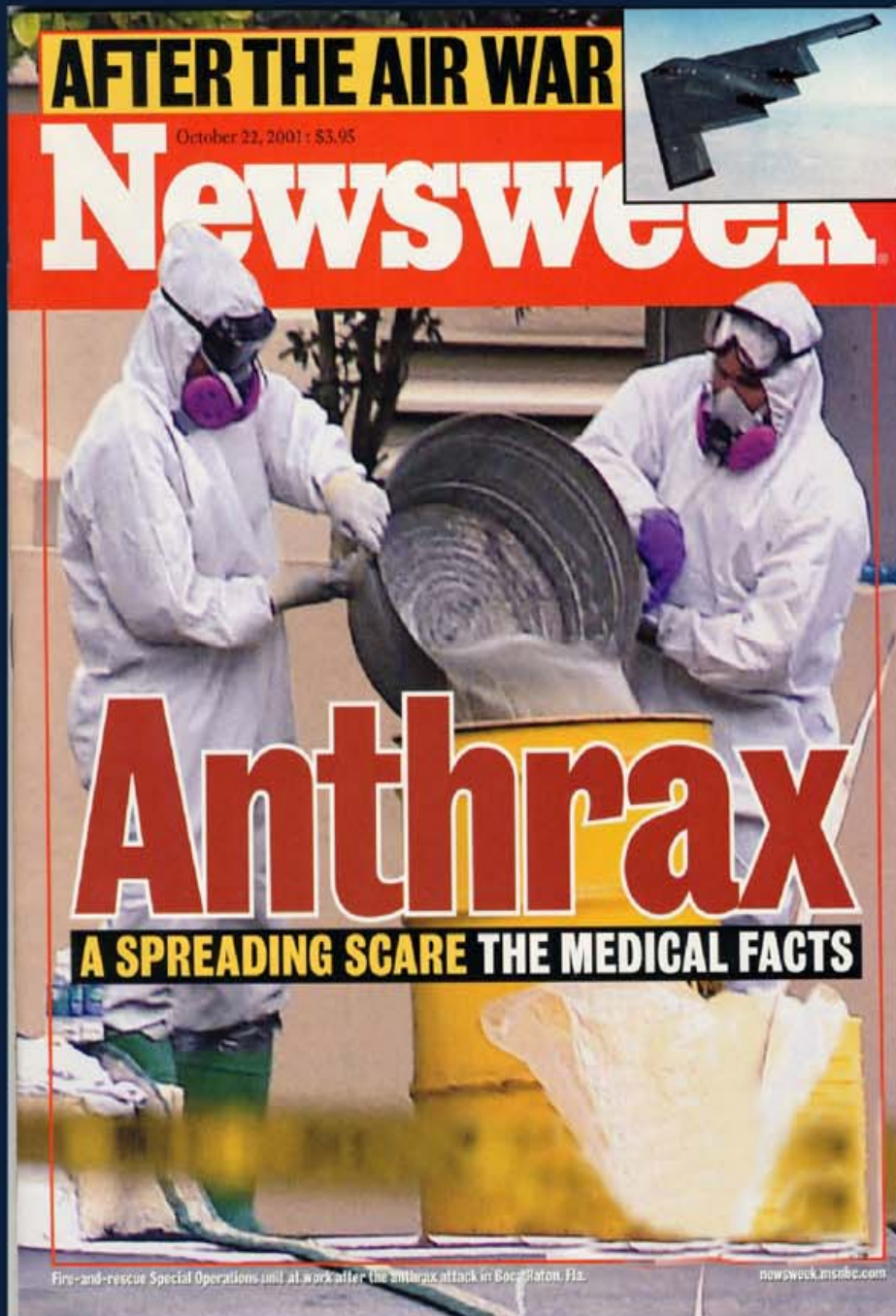
**Caroline Redmond, Martin J. Pearce,
Richard J. Manchee**

*Detection Department, CBD, Porton Down,
Salisbury SP4 0JQ, UK*

Bjorn P. Berdal

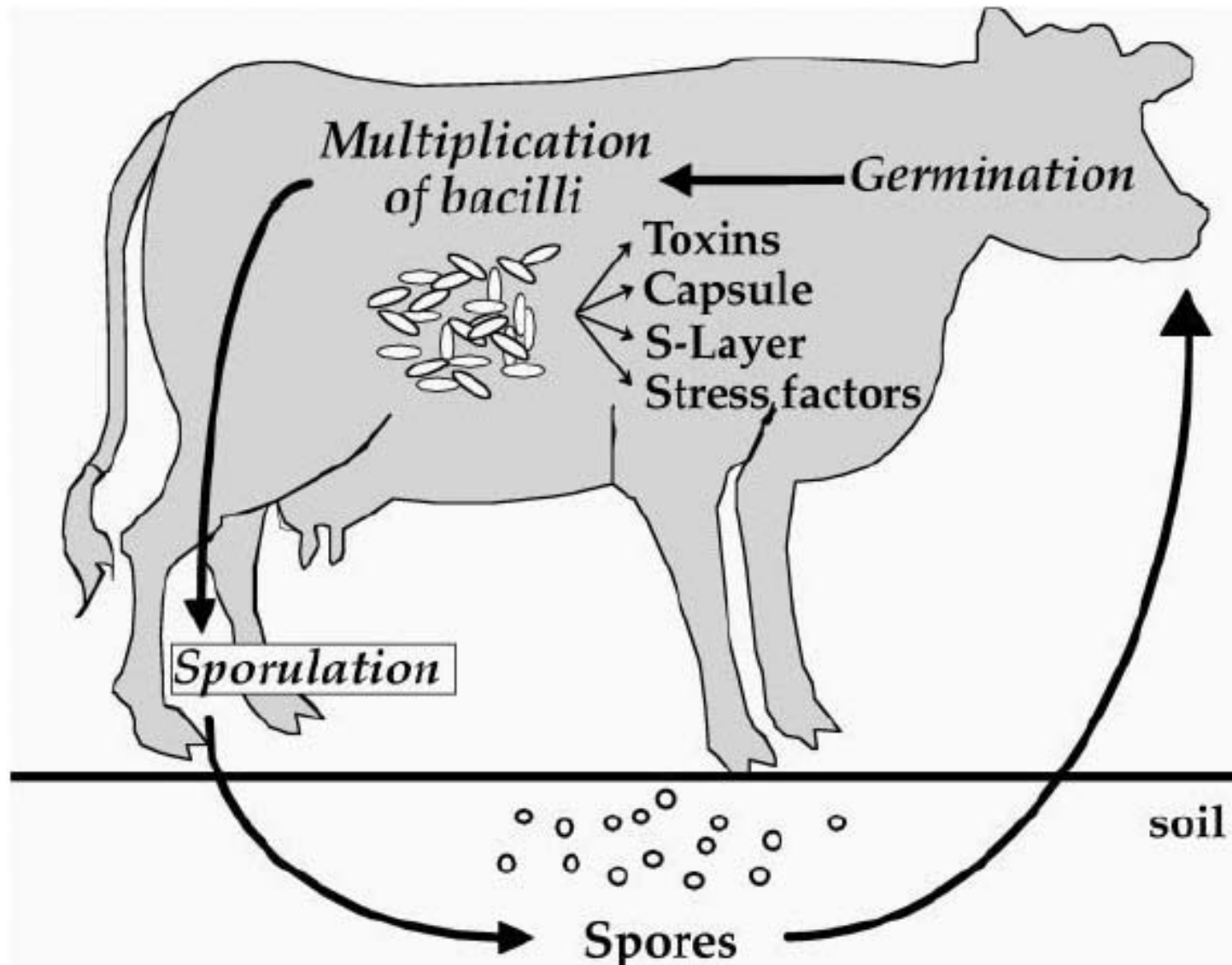
*Norwegian Defence Microbiology Institute,
PO Box 4302 Torshov, N-0401 Oslo, Norway*

Nature 1998; 393: 747-8





Bacillus anthracis cycle





Anthrax-infected Bison, Cananda



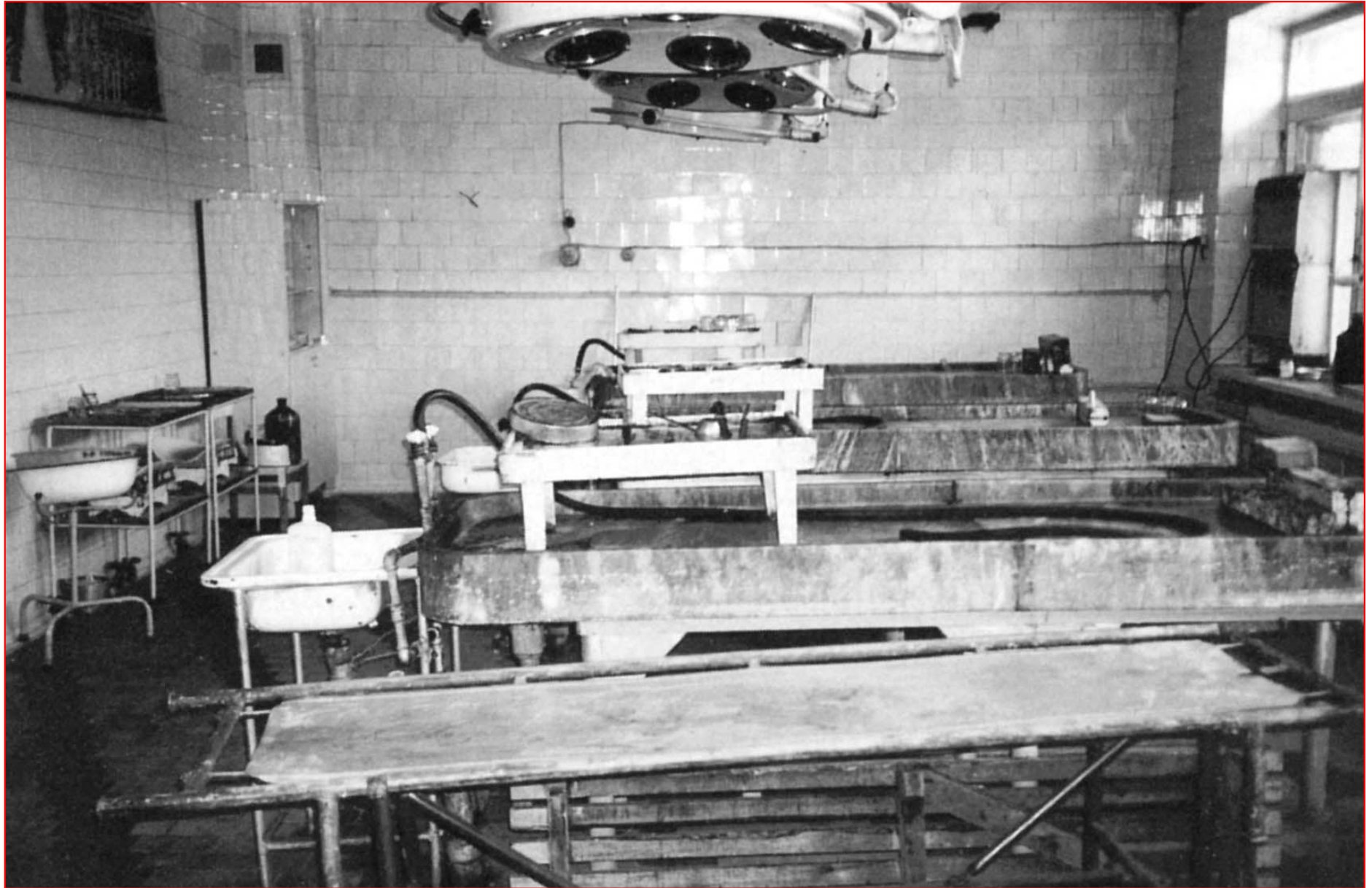


Goat wool sorting 1950 in the US





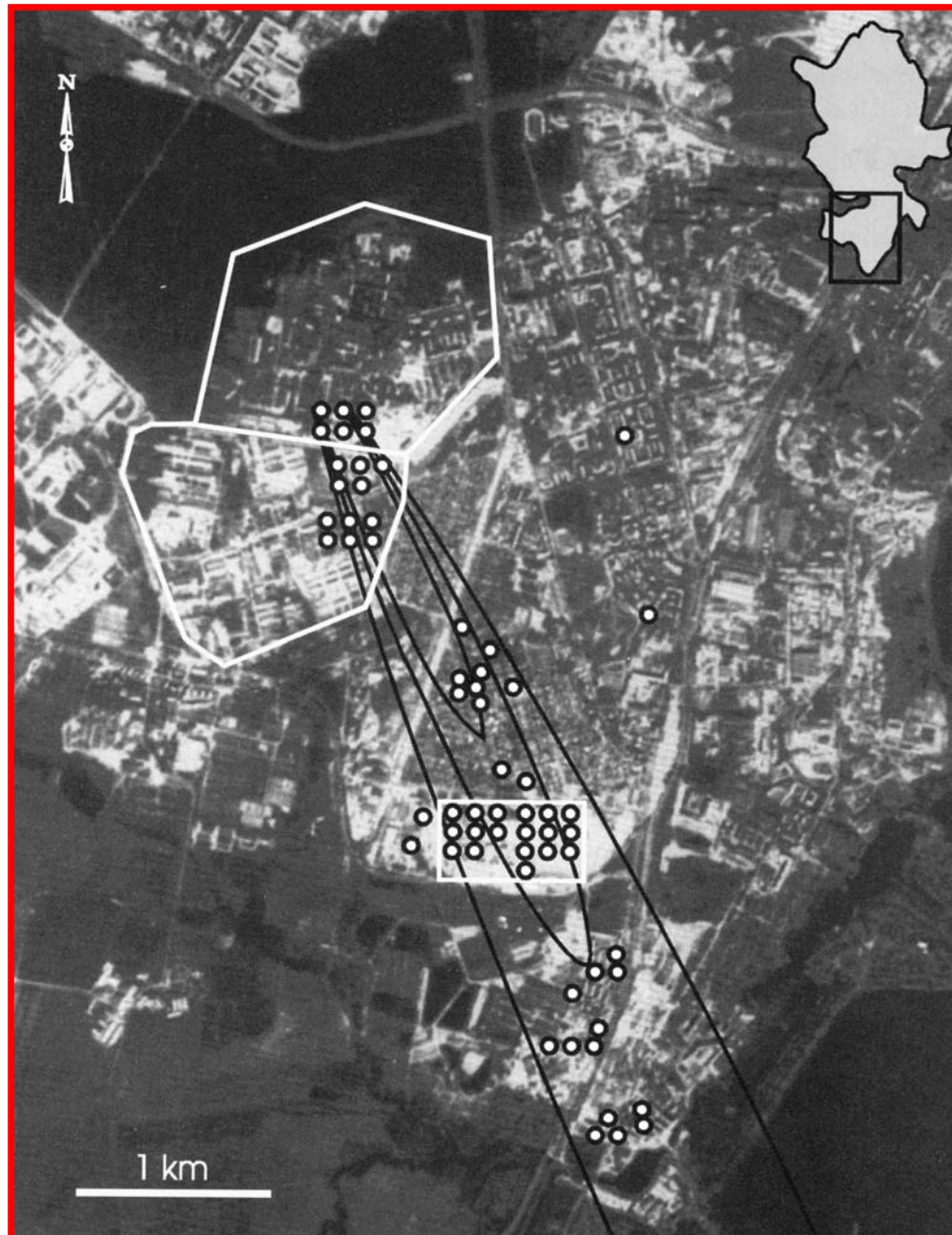
Autopsy room in Sverdlovsk



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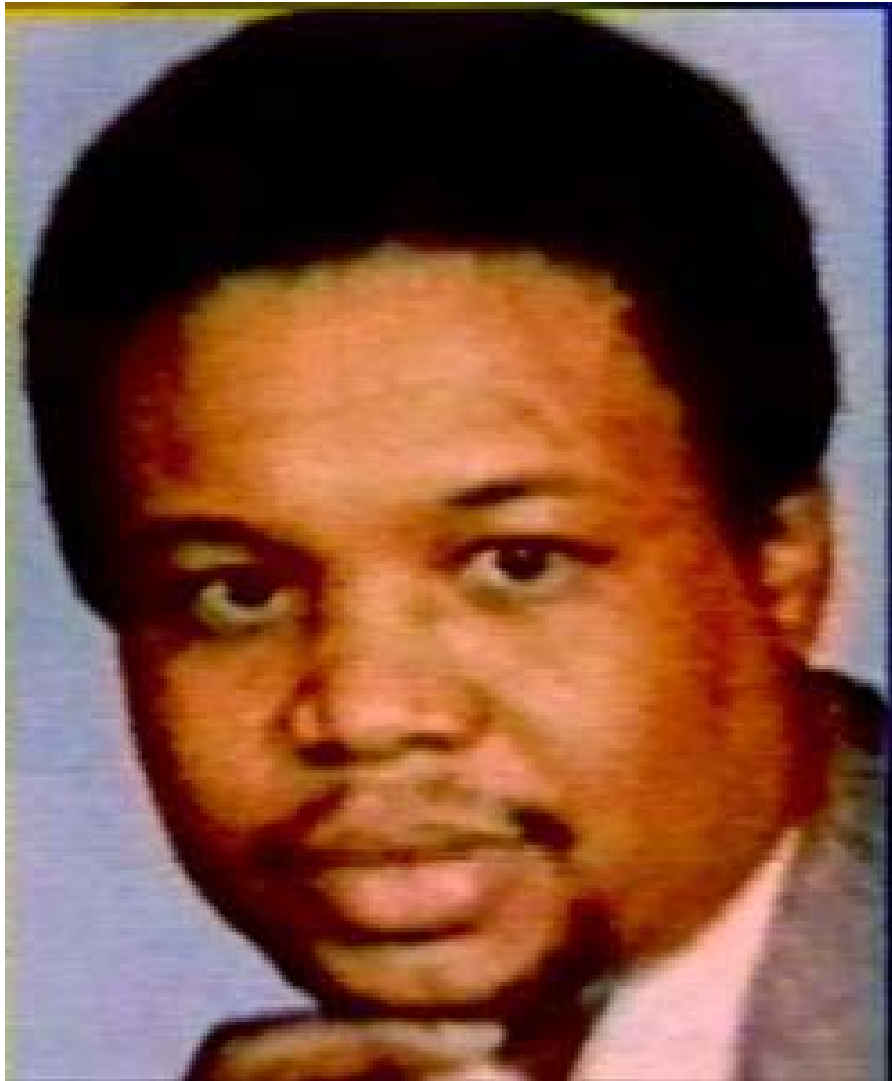


Anthrax case location





Fatal inhalation case



Postal worker Thomas Morris Jr.. Morris told 911 operators hours before he died of inhaled anthrax that he thought he had the disease, despite a doctor's dismissal, and recalled a co-worker handling a powder-containing letter a week earlier



Surviving inhalation case



Norma Wallace smiles at a news conference at Vitura Hospital when she was released from the hospital after being treated for inhalation anthrax. She said she wanted to remind Americans that ``there is hope" despite the anthrax crisis



94-year-old Ottillie Lundgren



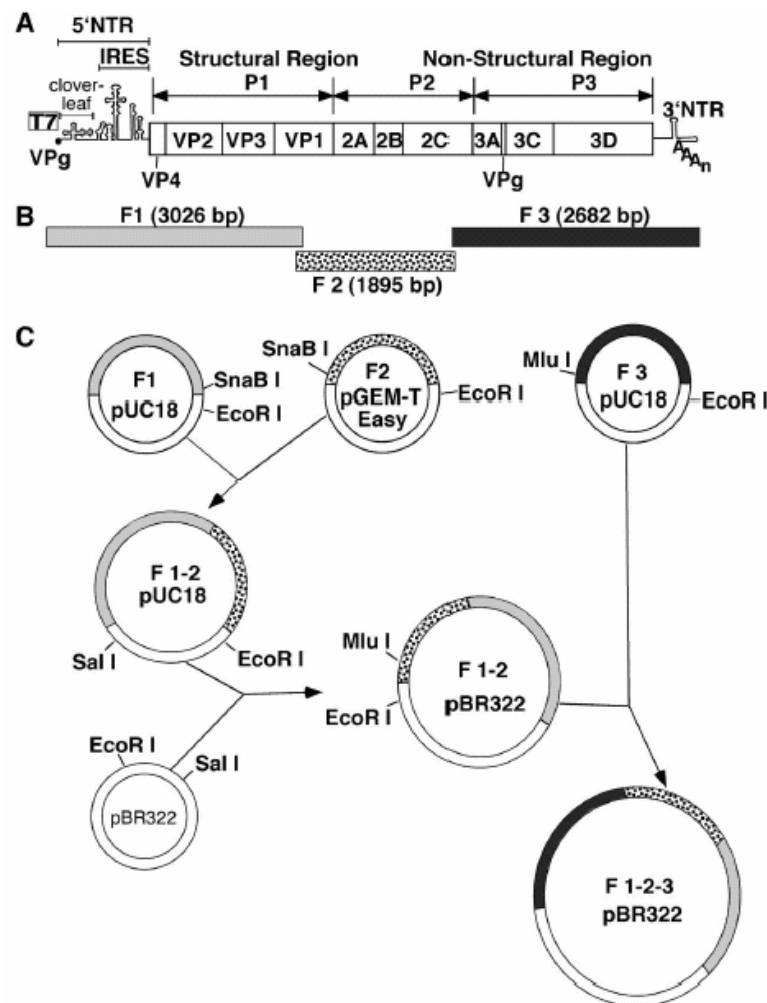
Authorities stand outside the house of a woman who has been hospitalized with what is believed to be inhalation anthrax Tuesday, Nov. 20, 2001. The woman, identified as 94-year-old Ottillie Lundgren, was admitted Friday a hospital with a respiratory ailment. Doctors initially suspected she had pneumonia.



Chemical Synthesis of Poliovirus cDNA: Generation of Infectious Virus in the Absence of Natural Template

Jeronimo Cello, Aniko V. Paul, Eckard Wimmer*

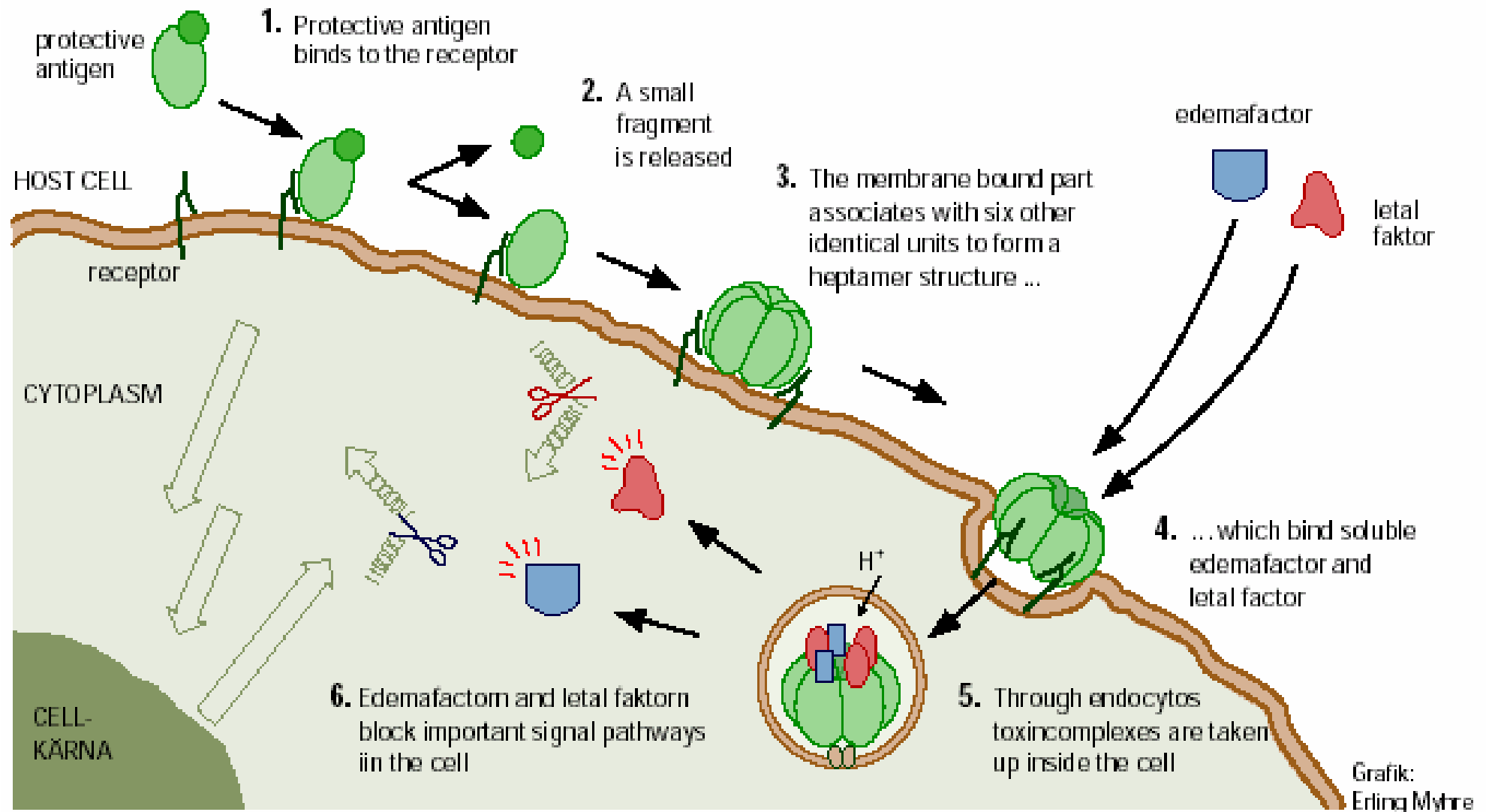
Department of Molecular Genetics and Microbiology, School of Medicine, State University of New York at Stony Brook, Stony Brook, NY 11794-5222, USA.



Full-length poliovirus cDNA was synthesized by assembling oligonucleotides of plus and minus strand polarity. The synthetic poliovirus cDNA was transcribed by RNA polymerase into viral RNA, which translated and replicated in a cell-free extract resulting in the de novo synthesis of infectious poliovirus. Experiments in tissue culture using neutralizing antibodies and CD155 receptor-specific antibodies and neurovirulence tests in *CD155* transgenic mice confirmed that the synthetic virus had biochemical and pathogenic characteristics of poliovirus. Our results show that it is possible to synthesize an infectious agent by in vitro chemical/biochemical means solely following instructions from a written sequence.



Anthrax pathogenesis



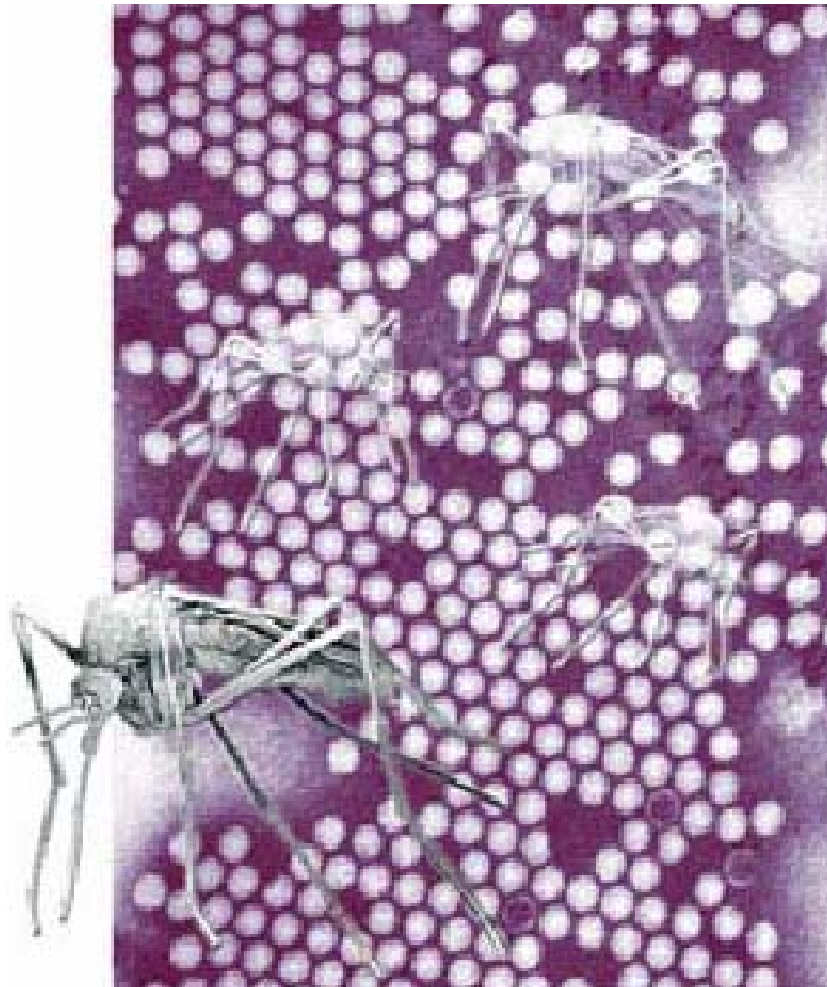


Intensive care beds a limited resource





West Nile Fever



MORE MOSQUITO MAYHEM: The list of symptoms now associated with West Nile virus includes a condition reminiscent of paralytic poliomyelitis. The background is an electron micrograph of the poliovirus.

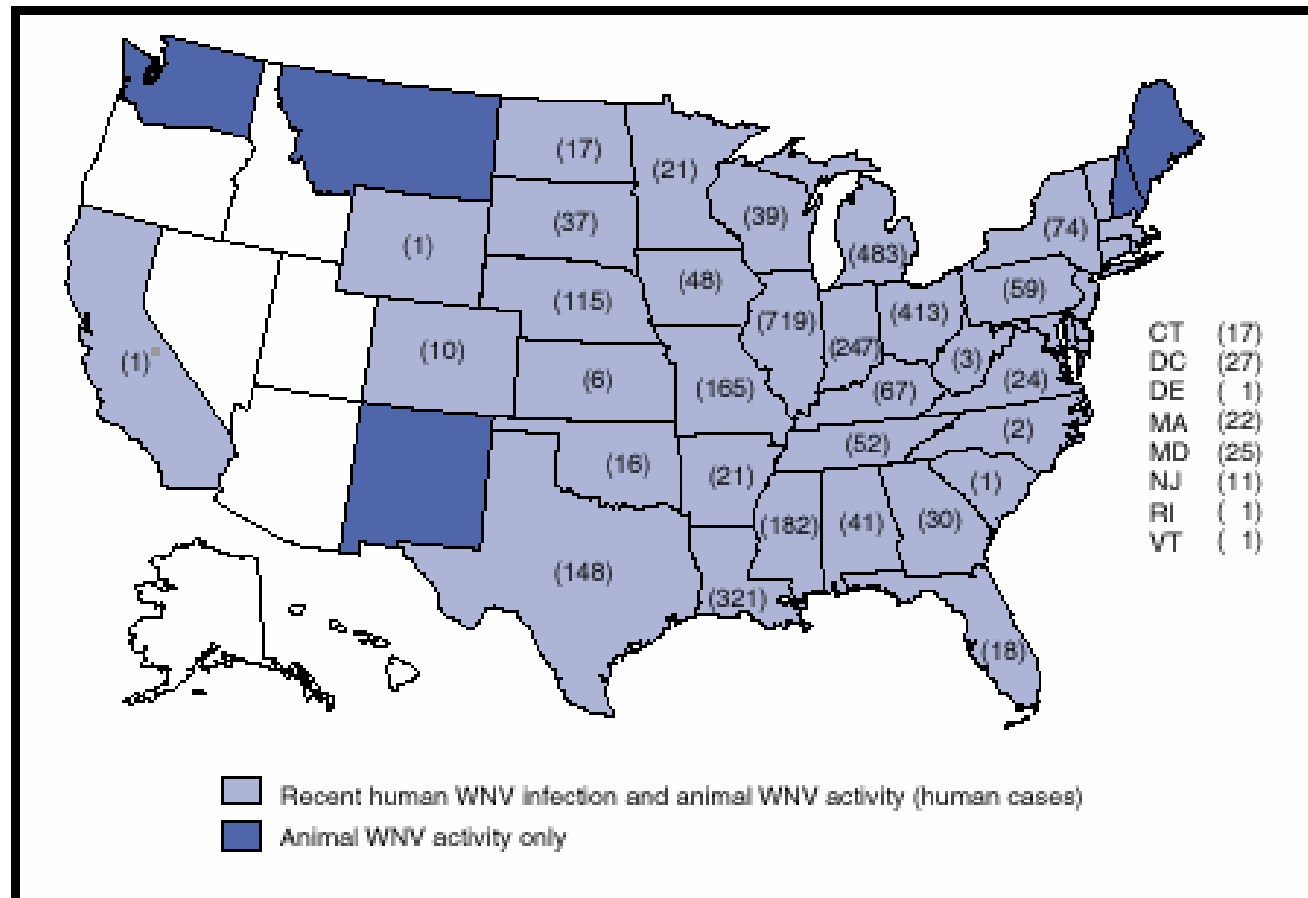
West Nile Mimics Polio

Electromyograms identified damaged motor neurons in the spinal cord's gray matter where poliovirus is found | By Ricki Lewis



US cases as of November 6, 2002

FIGURE. Areas reporting West Nile virus (WNV) activity — United States, 2002*



* As of 8 a.m. Mountain Standard Time, November 6, 2002.

† California has reported human WNV activity only.



Where did West Nile virus come from?

- The Centers for Disease Control & Prevention has admitted that it supplied Iraqi scientists with nearly two dozen viral and bacterial samples in the 1980s, including the plague, West Nile, and dengue fever.
- The CDC was abiding by WHO guidelines that encouraged the free exchange of biological samples among medical researchers says Thomas Monath, who headed the CDC lab where the viruses came from during the period in which they were handed over. "It was a very innocent request, which we were obligated to fulfill," recalls Monath. Plus, in the 1980s, Iraq and the U.S. were allies.
- The West Nile strain that so far has killed 46 people in the U.S. is not the same strain provided to Iraq. It is unlikely that it could have mutated. They also question whether terrorists would even try to develop West Nile as a weapon when more virulent viruses are available.



UK Company Offers Ebola Virus 'Kit' for Sale Over Internet

The formula and the genetic material required to produce one of the world's deadliest and most feared diseases are both available from British organisations over the internet.

Reporters last week bought several of the DNA strands necessary to create the highly contagious ebola virus from a company near Cambridge. Its DNA code - its recipe - was obtained from a website.

This comes amid fears that terrorists and rogue states will turn to bioterrorism, using viruses such as ebola, smallpox or anthrax, to bring chaos to Europe and America.



Local Transmission of *Plasmodium vivax* Malaria --- Virginia, 2002

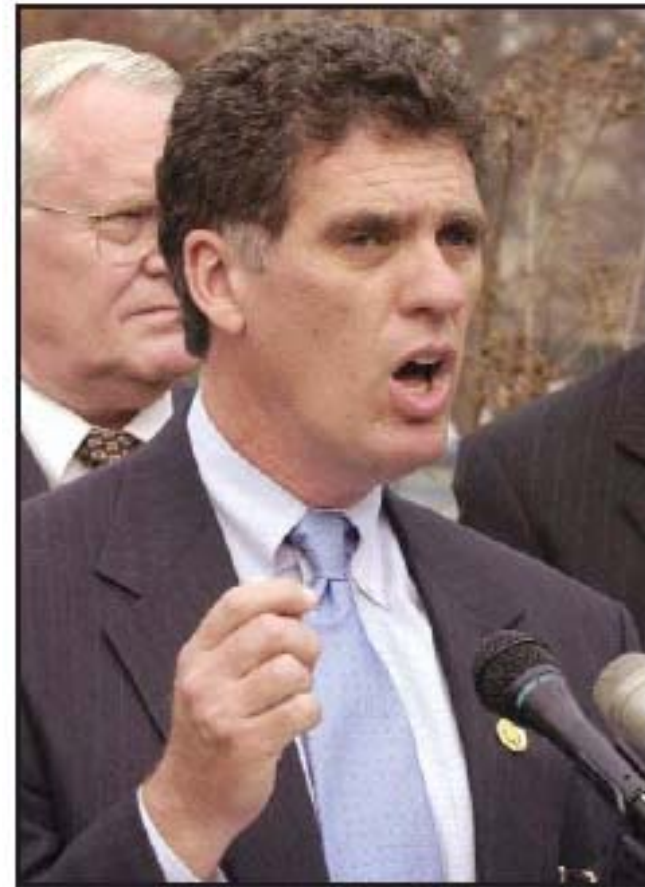
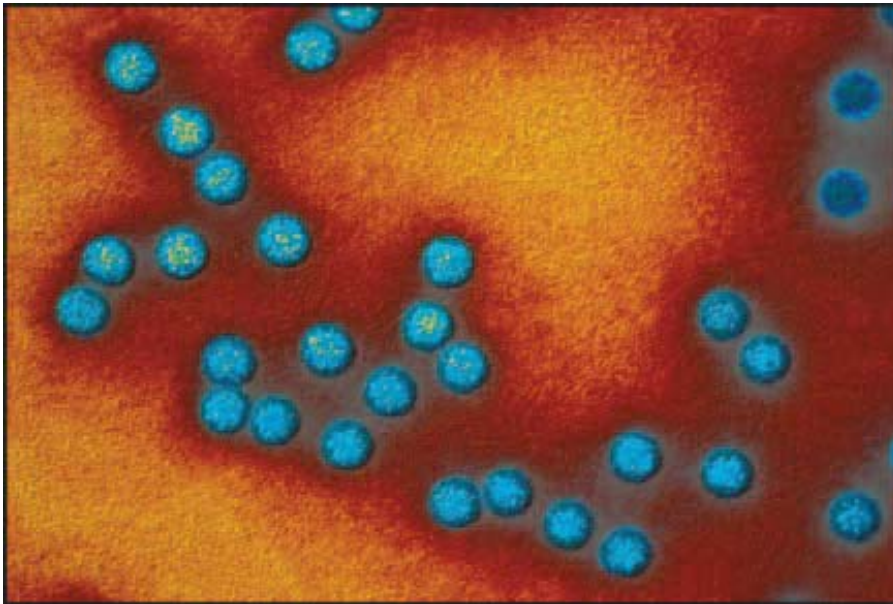
Malaria transmission in the United States was largely eliminated during the mid-20th century; however, sporadic cases of locally acquired mosquito-transmitted malaria continue to occur. Since 1997, four separate probable mosquito-transmitted malaria outbreaks have been reported to CDC, including one from Virginia.



Syntetic poliovirus

BIOTERRORISM

A Call for Restraint On Biological Data



Critic. Rep. Dave Weldon took AAAS to task for publishing a paper on poliovirus.



Scientists planning a new life form

By Justin Gillis, Washington Post, 11/21/2002

WASHINGTON - Scientists in Rockville, Md., are planning to create a new form of life in a laboratory dish, a project that raises ethical and safety issues but also promises to illuminate the fundamental mechanics of living organisms. Craig Venter, the gene scientist with a history of pulling off unlikely successes, and Hamilton Smith, a Nobel laureate, are behind the plan. Their intent is to create a singlecelled, partially man-made organism with the minimum number of genes necessary to sustain life. If the experiment works, the microscopic man-made cell will begin feeding and dividing to create a population of cells unlike any previously known to exist.

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Novel BW treats

- Genetically-engineered pathogens are qualitatively different from conventional BW agents
- Attributes may include one or more of the following
 - Safer handling & deployment
 - Easier propagation and/or distribution
 - Improved ability to target the host
 - Greater transmissivity and infectivity
 - More difficult to detect
 - Greater toxicity, more difficult to combat
 - More (self-limiting, self-enhancing...)



Binary Biological Weapons

- Analog of a binary chemical weapon
 - Two independent elements
 - Each safe to handle
 - Assembled before use
- Virus & helper virus
- Bacterial virulence plasmid examples
 - *Y. pestis*, *B. anthracis*, *S. dysenteriae*



Designer Genes & Life Forms

Synthetic genes and gene networks

- Combination strategies: DNA shuffling
- Synthetic viruses
 - ✓ Influenza antigen switching (N3/H6)
- Synthetic organism
 - ✓ Chimera & de novo design
 - ❖ Mycoplasma genitalum (541 genes)
 - ❖ Mycoplasma pneumoniae (677 genes)
 - ❖ Estimate 250-400 genes needed



Gene Therapy as a Weapon

- Goal: Permanent change in the genetic makeup
- Approach: Use transforming viruses of similar DNA vector carrying "Trojan horse" genes.
E.g. Retrovirus, adenovirus, poxvirus, HSV-1, etc.
- Potential for misuse
 - Intentional
 - Unintentional



Stealth Viruses

- Stealth virus is both transforming and conditional inducible
- The human chromosome is littered with viral and other remnants
- We harbor many transforming viruses
 - Herpes virus, cytomegalovirus, Epstein-Barr virus
 - SV40 contamination
- BW similar to gene therapeutic strategies, but require tighter control



Designer Diseases

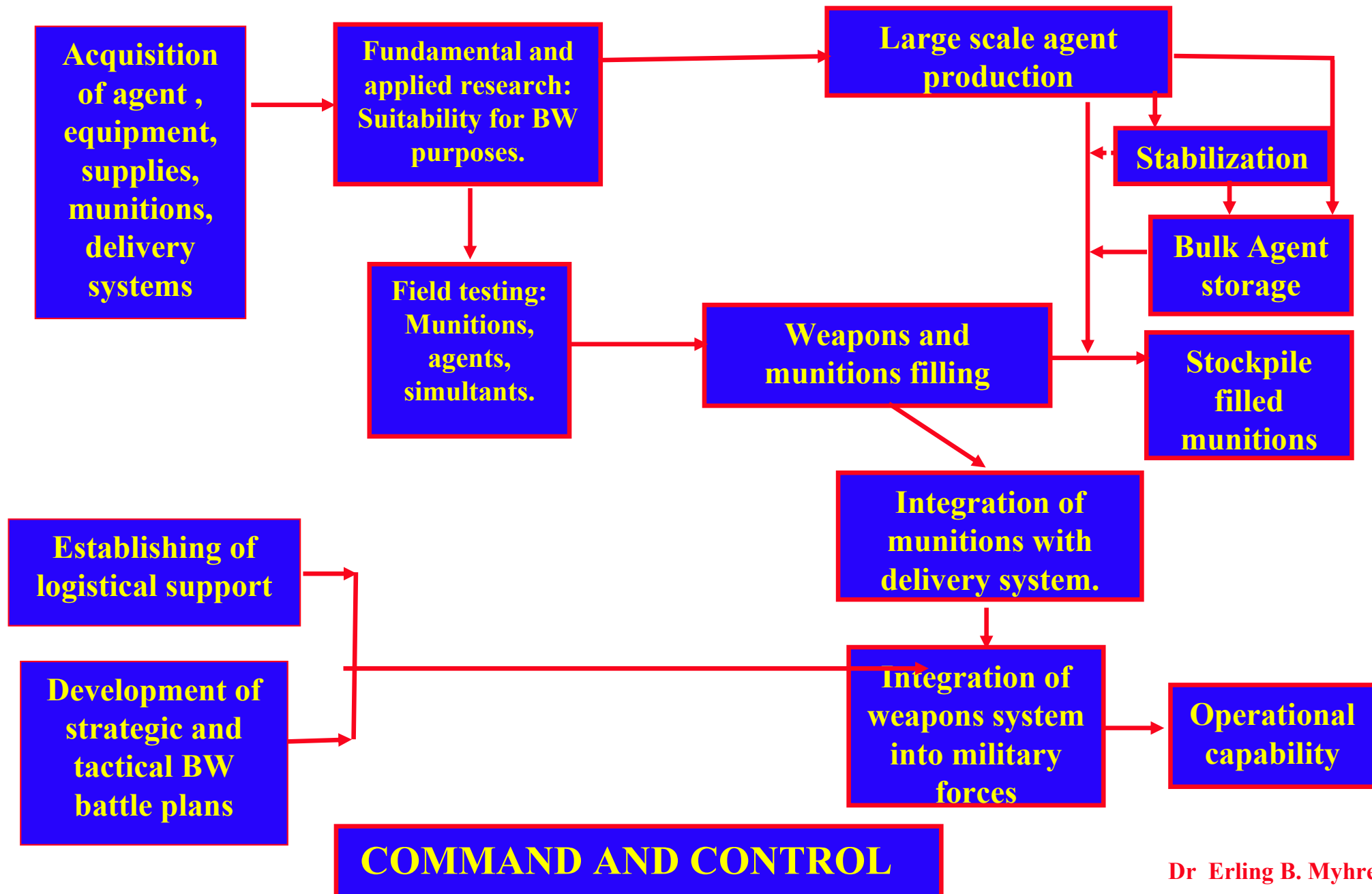
- Apoptosis: Programmed cell death
- Specific apoptosis surface receptors. Death receptors
 - e.g.: fas, TRAMP, TRAIL-R, TNF-R1
 - Most ligands not yet identified
 - Cytokine receptors
- General agonist would be lethal
- More "nuclear weapons", other signalling pathways

Destruction of Al Hakam, Iraq





Acquisition of a military capability

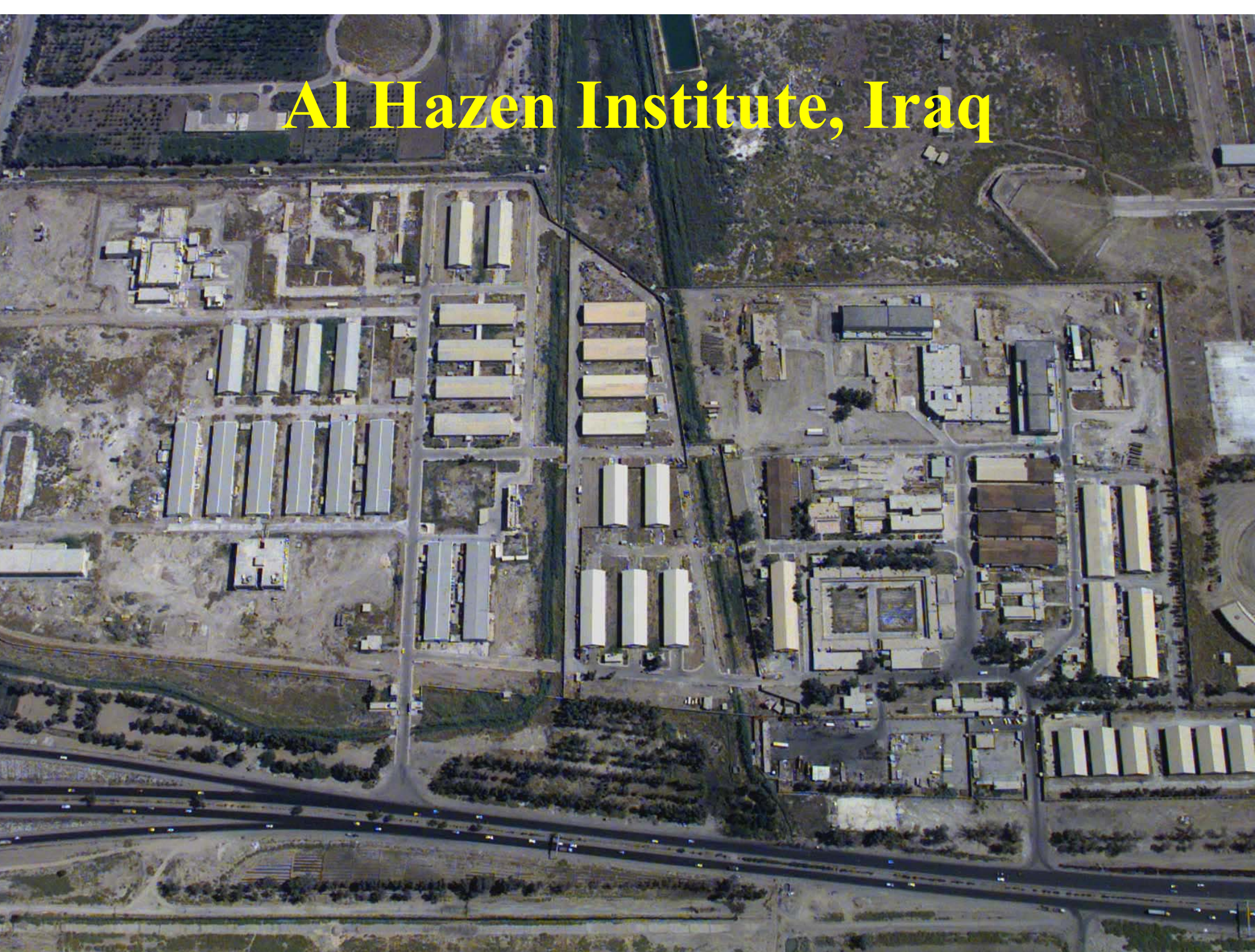




Olsa production line - Irak



Al Hazen Institute, Iraq





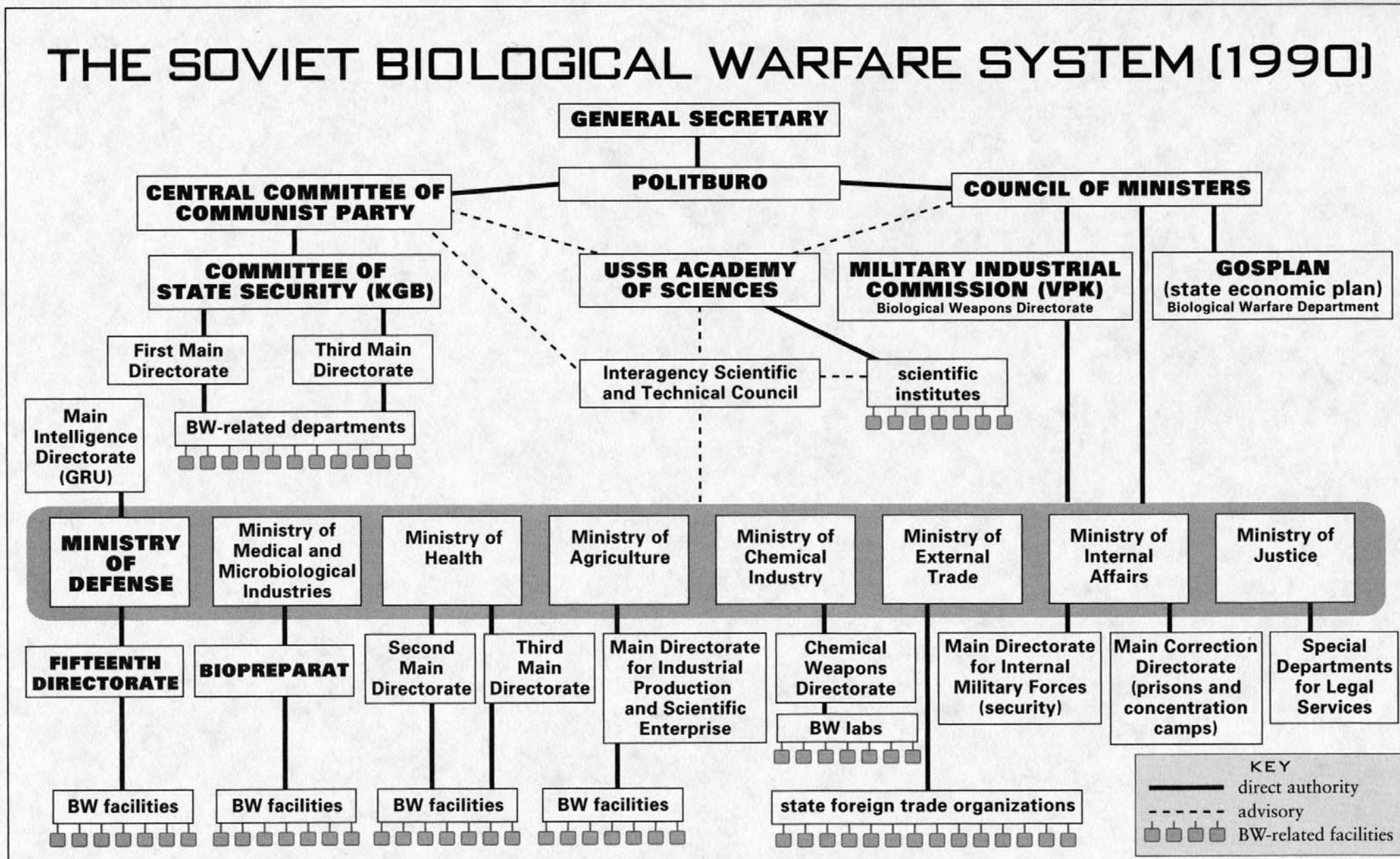
Steptnogorskt, Siberia



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Russian Biological Warfare Programme





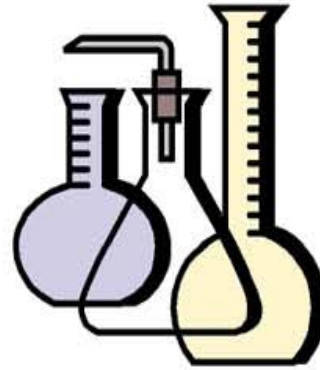
New research efforts



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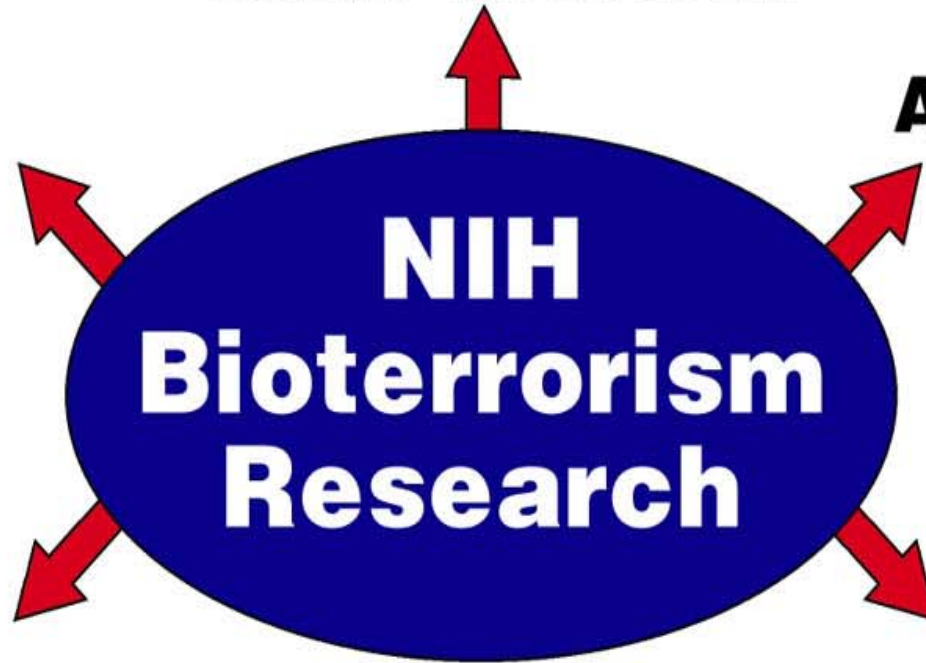
Genomics



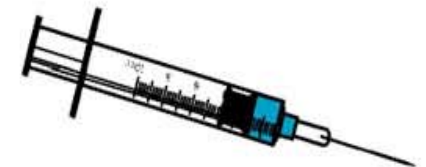
Basic Research



Antimicrobials



Diagnostics



Vaccines




Automated DNA sequencing





Gene arrays methodologies

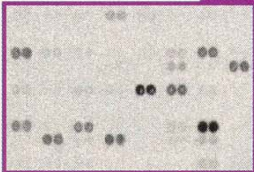
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SIGMA
GENOSYS

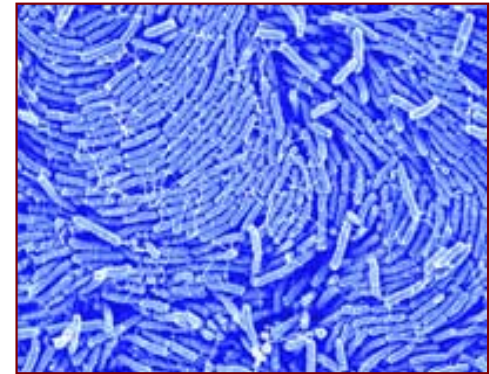
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Universal classifier detects bacteria in space--and on the homeland



**ON THE HORIZON:
New technologies will
protect the health of
astronauts on long
space flights**



Bacteria magnified 2,500 X

Researchers at the National Space Biomedical Research Institute (NSBRI) are developing technologies to identify and monitor anticipated and unanticipated microorganisms in space--technologies, they suggest, that could also help to more efficiently diagnose medical conditions down here on Earth, as well as help detect biological hazards in this post-Sept. 11 world

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Stricter rules for dangerous pathogens

Today's World: Research vs. Security

Investigators find it increasingly difficult to obtain bacterial pathogens for antibioterrorism studies | [By Dana Wilkie](#)

Nearly three years ago, the federal government gave **Nancy Connell** the green light to investigate how people respond to infection by *Bacillus anthracis*, the bacterial agent that causes anthrax. With \$3 million (US) from the Department of Defense, Connell hoped to learn how to detect the bacteria within hours of infection. But thanks to the hurdles put in her path, it took until this past July for Connell to get her hands on the bacterial strain for her study. Today, her team at the Center for BioDefense at the University of Medicine and Dentistry of New Jersey works 12-hour days to make up for lost time.

Syndromic Surveillance for Bioterrorism Following the Attacks on the World Trade Center --- New York City, 2001

Immediately after the September 11, 2001, terrorist attacks on WTC, the New York City Department of Health and Mental Hygiene was concerned about the possibility of a secondary attack with a biologic agent. Because communications was lost as a result of the attacks, concern arose that this disruption would affect the ability to recognize a bioterrorist event and, a syndromic surveillance system was quickly implemented in hospital emergency departments to identify a large-scale bioterrorist event.



What next?





Effective BW inspections



